

Toxic dilatation of the colon

A. Barney Hawthorne

Abstract

Toxic dilatation of the colon is a complication of acute severe ulcerative colitis, often at initial presentation or early in the disease course. It can also occur in Crohn's disease and infective colitis, particularly *Clostridium difficile* colitis. It is important to recognize and initiate prompt treatment to avoid perforation and peritonitis. The condition has a high mortality, particularly with fulminant *C. difficile*. In ulcerative colitis, more than half of those with toxic dilatation respond to medical treatment and avoid colectomy. Multidisciplinary management, encompassing daily input from medical and surgical specialties, is needed to determine whether emergency colectomy is required; this can often be a difficult decision. Nevertheless, delayed colectomy results in a greatly increased risk of peritonitis and poor postoperative outcomes.

Keywords *Clostridium difficile*; colectomy; colitis; ischaemic colitis; MRCP; toxic megacolon; ulcerative

Definition and incidence

Toxic dilatation of the colon, also known as toxic megacolon (TM), is a serious complication of colonic inflammation. It is seen most often in acute severe ulcerative colitis (UC) and Crohn's colitis, and much less often in association with other infective and inflammatory disorders (Table 1). It is defined as marked dilatation of the colon associated with signs of systemic toxicity (including fever, neutrophil leucocytosis, falling albumin, high C-reactive protein, hypotension and tachycardia).¹ Although a colonic diameter >5.5 cm is frequently considered as a feature of TM, this also occurs in the context of other disorders such as pseudo-obstruction in the absence of signs or symptoms consistent with systemic toxicity.

Many of the data derive from the pre-biological agent era and relate to inflammatory bowel disease (IBD). However, it is likely that the incidence of TM has fallen in recent years, probably related to earlier and more aggressive medical therapy.² TM occurs in 5–10% of patients admitted with IBD, more commonly with UC (10%) than Crohn's disease (2.3%).² In IBD, it is far more common in recently diagnosed colitis (60% of cases occurring in the first 3 years),³ usually in individuals with pancolitis. In non-IBD conditions, it is probably seen most often in *Clostridium difficile* colitis, where TM has a very high mortality of up to 67%⁴ because of concomitant co-morbidities and frailties in patients developing this infection.

A. Barney Hawthorne DM FRCP is Consultant Gastroenterologist at the University Hospital of Wales, Cardiff, UK. Competing interests: none declared.

Key points

- Toxic dilatation is a serious complication of colitis, with a high risk of peritonitis and death if not recognized and treated early
- It can occur as a complication of ulcerative colitis, Crohn's disease or any other cause of severe colonic inflammation
- It can be caused by drugs that slow colonic motility, or by overdistension of the colon, in patients with colitis
- Aggressive treatment of colitis, close monitoring of the degree of dilatation with surgical and medical input, and early colectomy if rapid improvement does not occur are essential to prevent colonic perforation

Aetiology and pathology

TM occurs in severe colitis and is associated with ulceration extending into the muscle layers; this produces marked interruption of normal colonic motility, resulting in paralysis and dilatation. There is evidence for a role of nitric oxide, as segments of dilated colon have higher levels of inducible nitric oxide synthase. In animal models, treatment with antibiotics or dexamethasone reduces nitric oxide synthase levels and the degree of dilatation.

It has been postulated that the mechanical effect of dilatation, deep ulceration and increased capillary permeability increases the risk of bacterial translocation into the circulation. In individuals undergoing colectomy for acute severe UC, cytomegalovirus (CMV) infection is more frequently found in patients with TM compared with those without dilatation.⁵ It is possible that CMV predisposes to TM, but seems more likely that CMV is seen more often in the most severe colitis.

Clinical features

TM in acute severe UC often occurs at the first presentation, with severe bloody diarrhoea and systemic upset. Abdominal pain is often present, but absence of pain does not rule out TM. A plain abdominal radiograph is essential to screen for evidence of colonic dilatation – often in the transverse colon where air accumulates when the individual is supine. Dilatation >5.5 cm or signs of thumb-printing (deep mucosal ulceration leaving islands of inflamed tissue outlined by air) suggest TM (Figure 1). Blood tests indicate anaemia, raised platelets, neutrophil leucocytosis, high C-reactive protein, perhaps with low serum potassium, phosphate and magnesium, and falling albumin (although the latter is not always evident in very acute presentations and can take several days to develop). In acute severe colitis, the colon is usually empty, and routine daily abdominal films are not required unless there is dilatation on the initial film. TM can develop after several days of treatment in patients failing to respond to intravenous (i.v.) corticosteroid treatment, and abdominal films must be repeated if there is worsening pain or abdominal distension. An abdominal CT scan gives much more

Underlying diseases and medications associated with toxic dilatation of the colon

Inflammatory bowel disease	Ulcerative colitis Crohn's colitis
Infection	<i>Clostridium difficile</i> Amoebic dysentery Disseminated cytomegalovirus <i>Shigella</i> <i>Salmonella</i> <i>Campylobacter</i> <i>Aspergillus</i> <i>Cryptosporidiosis</i> <i>Yersinia</i> Haemolytic–uraemic syndrome (complicating <i>Escherichia coli</i> O157 infection)
Other disorders	Ischaemic colitis Diverticulitis Obstructing colonic carcinoma Colonic volvulus
Factors associated with triggering or worsening of toxic dilatation	Opioids (including loperamide) 5-HT ₃ antagonists Anticholinergics Hypokalaemia Hypomagnesaemia Overdistension at colonoscopy Overdistension during radiology Chemotherapy

Table 1



Figure 1 Abdominal radiograph with dilated transverse colon demonstrating multiple mucosal islands (thumb-printing). The descending and sigmoid colon are collapsed, but a thickened wall can be clearly seen.



Figure 2 Abdominal computed tomography scan showing dilatation of the caecum and transverse colon, with undermining ulcers along the wall.

information on the colon (Figure 2), and can rule out perforation or other extracolonic pathology.

Treatment of toxic megacolon in acute severe ulcerative colitis

Prevention is the most important consideration. In patients with suspected acute severe UC, opioids (including analgesics and loperamide), 5-hydroxytryptamine (5-HT₃) antagonists (e.g. ondansetron) and anticholinergics must be avoided because they can reduce colonic motility.

Some patients already have a confirmed diagnosis of UC, but this can also be a first presentation. Stool cultures must always be taken, and if UC is suspected, corticosteroids (i.v. methylprednisolone 60 mg daily or i.v. hydrocortisone 100 mg 6-hourly) must be started promptly, and not delayed pending stool culture results (which can take several days for confirmed negative results).

Flexible sigmoidoscopy is often needed to confirm the diagnosis or severity of colitis. This must be done gently, avoiding excessive insufflation and using carbon dioxide rather than air as patients have a heightened risk of iatrogenic perforation. Biopsies should be taken and include urgent assessment for CMV. Multiple inclusion bodies should trigger treatment with IV ganciclovir. Colonoscopy often adds little further information and should be avoided unless there are very specific reasons to evaluate the right colon, in which case it must be done by an expert colonoscopist. Early dilatation should trigger a joint senior medical gastroenterology and colorectal surgical assessment.

Emergency colectomy is indicated if there is evidence of peritonitis, perforation documented by radiology, or severe pain with shock or a high National Early Warning Score (NEWS). In at least half of patients, it is possible to avoid colectomy using close monitoring, high-dose i.v. corticosteroids, prophylactic low-molecular-weight heparin, correction of dehydration or abnormal electrolytes (particularly potassium, phosphate and

magnesium) and oral nutrition. Daily review by both medical and surgical teams should continue. Antibiotic cover (i.v.) for coliforms is appropriate.

If by day 3 of i.v. corticosteroid treatment there is no significant response, rescue therapy with infliximab or i.v. ciclosporin can be considered, after surgical review and with agreement that immediate emergency colectomy is not needed. Continuing clinical deterioration, with lack of or worsening resolution of dilatation, increasing pain, continuing fever, haemodynamic deterioration and peripheral oedema with rapidly falling albumin are indications for colectomy. Delaying surgery in this context greatly increases the risk of surgical complications, and the goal must be to avoid perforation, which always represents a failure of management.

Treatment of toxic dilatation in other causes of colitis

Patients admitted with acute bloody diarrhoea have a broad differential diagnosis, including IBD, infective colitis and, in older patients, ischaemic colitis. Urgent stool cultures should be sent for analysis; at least two samples for *C. difficile* must be taken. Corticosteroid treatment should be started if IBD is suspected, but should be stopped once an infective cause has been confirmed. Similarly, corticosteroids have no role in ischaemic colitis. Prompt antibiotic treatment must be commenced, with appropriate microbiology advice. Oral vancomycin 125 mg four times daily is used for fulminant *C. difficile* colitis, with i.v.

metronidazole added if oral absorption is likely to be poor. *Campylobacter* should be treated with azithromycin 500 mg daily for 3 days. Individuals with UC are often fit and healthy before the onset of acute severe colitis, and if TM develops are more likely to tolerate a few days of intensive medical therapy. In TM resulting from *C. difficile* and other causes, often in frail elderly patients, the decision to operate must be taken at an earlier stage, recognizing the lack of physiological reserves and the likely rapid deterioration in the face of sepsis. ◆

KEY REFERENCES

- 1 Jalan KN, Sircus W, Card WI, et al. An experience of ulcerative colitis. I. Toxic dilation in 55 cases. *Gastroenterol* 1969; **57**: 68–82.
- 2 Gan SI, Beck PL. A new look at toxic megacolon: an update and review of incidence, etiology, pathogenesis, and management. *Am J Gastroenterol* 2003; **98**: 2363–71.
- 3 Sheth SG, LaMont JT. Toxic megacolon. *Lancet* 1998; **351**: 509–13.
- 4 Hookman P, Barkin JS. Clostridium difficile associated infection, diarrhea and colitis. *World J Gastroenterol* 2009; **15**: 1554–80.
- 5 Criscuolo V, Rizzuto MR, Gallo E, Orlando A, Cottone M. Toxic megacolon and human Cytomegalovirus in a series of severe ulcerative colitis patients. *J Clin Virol* 2015; **66**: 103–6.

TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online [here](#).

Question 1

A 28-year-old man presented with diarrhoea eight times a day with bloody liquid stool. He had recently been found at colonoscopy to have ulcerative colitis. He had been admitted 3 days earlier having failed to respond to 1 week of prednisolone 40 mg daily.

On clinical examination, there was marked abdominal tenderness.

Investigations

- Haemoglobin 120 g/litre (130–180)
- C-reactive protein 60 mg/litre (<10)
- Serum albumin 32 g/litre (37–49)
- Plain abdominal X-ray showed a 7 cm dilated transverse colon

What is the most appropriate management at this stage?

- Emergency colectomy
- Intravenous infliximab
- Methylprednisolone
- Continue oral prednisolone and add intravenous broad-spectrum antibiotics
- Oral antibiotics

Question 2

A 24-year-old woman was admitted with confusion and diarrhoea. She had a 2-week history of bloody diarrhoea treated initially as gastroenteritis at a small local hospital. However, stool cultures were negative and flexible sigmoidoscopy had shown typical features of ulcerative colitis with deep ulceration in the rectum and sigmoid.

On clinical examination, she was drowsy. Her temperature was 38.5°C, heart rate 120 beats/minute, and systolic blood pressure 80 mmHg. There was severe abdominal tenderness with guarding.

Investigations

- Serum albumin 22 g/litre (37–49)
- C-reactive protein 80 mg/litre (<10)
- CT scan of the abdomen showed 6 cm dilated right colon and transverse colon, with deep ulceration and gas within the colonic wall

What is the best management for this patient with toxic megacolon?

- Emergency colectomy
- Intravenous methylprednisolone
- Intravenous infliximab
- Intravenous broad-spectrum antibiotics
- Insertion of a rectal tube

Question 3

A 79-year-old man presented with abdominal pain and distension. He had been treated for 3 weeks for pneumonia on a background of chronic obstructive airways disease. He was also being treated for acute lower back pain caused by a T12 vertebral collapse. He had developed severe diarrhoea, and sigmoidoscopy the day before had shown severe inflammation with yellowish raised nodules covering the rectal and sigmoid mucosa, with the appearance of sweetcorn. He had been taking codeine phosphate 60 mg 6-hourly for his back pain for the previous week.

Investigation

- Plain abdominal X-rays show transverse colon dilated to 7 cm

What is the best immediate management?

- A Corticosteroids intravenously
- B Vancomycin orally
- C Emergency colectomy
- D Supportive measures
- E Infliximab intravenously